SUPPORTING INFORMATION – for publication

Number of ligands	228
Number of rotatable torsions of ligands: Maximum Minimum Average	 32 0 9
Number of heavy atoms of ligands: Maximum Minimum Average	 73 6 25
Molecular weights of ligands: Maximum Minimum Average	 950 88 362

Table S1. Properties of ligands in the PDBbind core set of complexes.

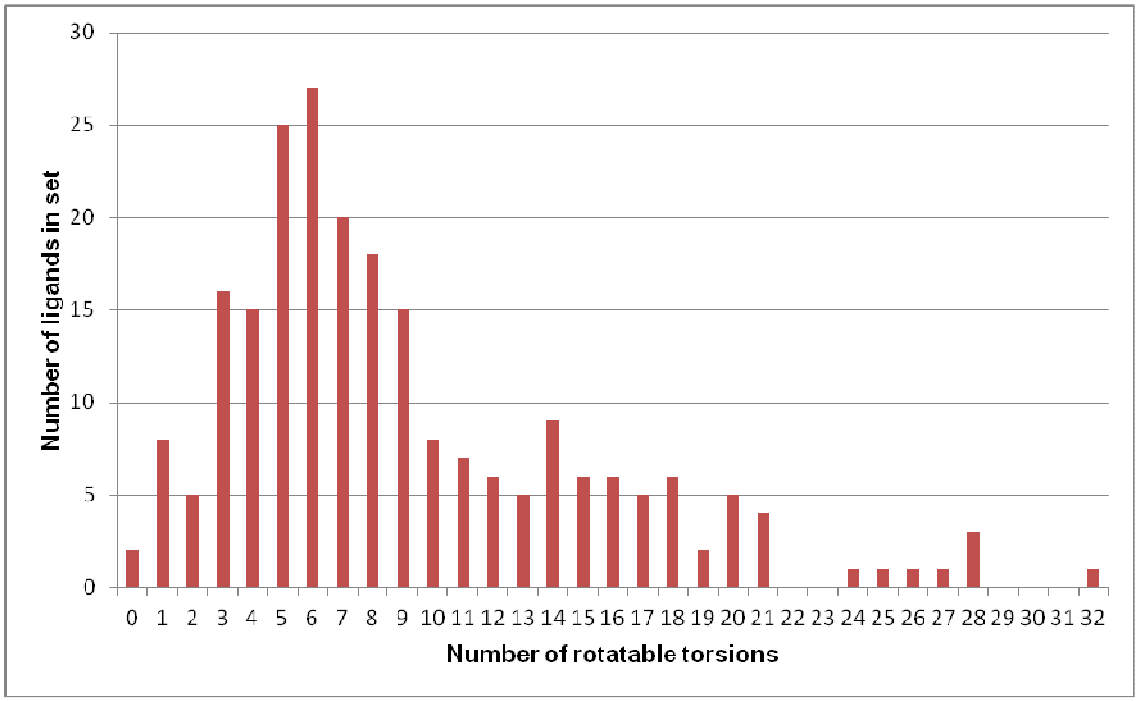

Figure S1. Distribution of flexibility in ligand set.

The following Korn Shell code was part of a script used to automate DOCK execution; it lists all the DOCK parameter settings used:

```
print "${arglist[${argno}]%.*}_noH.ms
R
X
0.0
4.0
1.4
${arglist[${argno}]%.*}_noH_site.sph" > INSPH


print "Y
10
${arglist[${argno}]%.*}_selected_spheres.sph
1
${arglist[${argno}]%.*}_noH_box.pdb" > showbox.in


print "${arglist[${argno}]%.*}_selected_spheres.sph
1
N
sphgen_cluster.pdb" > showsphere.in


print "compute_grids                  yes
grid_spacing                0.3
output_molecule             no
contact_score               yes
energy_score                yes
energy_cutoff_distance      9999
atom_model                  a
attractive_exponent         6
repulsive_exponent          12
distance_dielectric         yes
dielectric_factor           4
bump_filter                 yes
bump_overlap                0.75
receptor_file               ${arglist[${argno}]%.*}_H.mol2
box_file                    ${arglist[${argno}]%.*}_noH_box.pdb
vdw_definition_file         vdw_AMBER_parm99.defn
score_grid_prefix           grid
contact_cutoff_distance     4.5" > grid.in


print "ligand_atom_file
${ligid}_OBH.mol2
limit_max_ligands                                       no
skip_molecule                                           no
read_mol_solvation                                      no
calculate_rmsd                                          no
use_database_filter                                     no
orient_ligand                                           yes
automated_matching                                      yes
receptor_site_file
${arglist[${argno}]%.*}_selected_spheres.sph
max_orientations                                        10000
critical_points                                         no
chemical_matching                                       no
use_ligand_spheres                                      no
use_internal_energy                                     yes
```

```
internal_energy_rep_exp                                 12
flexible_ligand                                         yes
user_specified_anchor                                   no
limit_max_anchors                                       no
min_anchor_size                                         5
pruning_use_clustering                                  yes
pruning_max_orients                                     1000
pruning_clustering_cutoff                               100
pruning_conformer_score_cutoff                          25.0
use_clash_overlap                                       yes
clash_overlap                                           0.5
write_growth_tree                                       no
bump_filter                                             yes
bump_grid_prefix                                        grid
max_bumps_anchor                                        12
max_bumps_growth                                        12
score_molecules                                         yes
contact_score_primary                                   no
contact_score_secondary                                 no
grid_score_primary                                      yes
grid_score_secondary                                    no
grid_score_rep_rad_scale                                1
grid_score_vdw_scale                                    1
grid_score_es_scale                                     1
grid_score_grid_prefix                                  grid
dock3.5_score_secondary                                 no
continuous_score_secondary                              no
descriptor_score_secondary                              no
gbsa_zou_score_secondary                                no
gbsa_hawkins_score_secondary                            no
amber_score_secondary                                   no
minimize_ligand                                         yes
minimize_anchor                                         yes
minimize_flexible_growth                                yes
use_advanced_simplex_parameters                         no
simplex_tors_premin_iterations                          10
simplex_max_cycles                                      1
simplex_score_converge                                  0.1
simplex_cycle_converge                                  1.0
simplex_trans_step                                      1.0
simplex_rot_step                                        0.1
simplex_tors_step                                       10.0
simplex_anchor_max_iterations                           1000
simplex_grow_max_iterations                             500
simplex_grow_tors_premin_iterations                     0
simplex_random_seed                                     0
simplex_restraint_min                                   no
atom_model                                              all
vdw_defn_file
vdw_AMBER_parm99.defn
flex_defn_file                                          flex.defn
flex_drive_file                                         flex_drive.tbl
ligand_outfile_prefix
${ligid}${jobaddon}
write_orientations                                      no
num_scored_conformers                                   1
rank_ligands                                            no" > dock6.in
```